CGP77675

Cat. No.: HY-W062835

CAS No.: 234772-64-6

Molecular Formula: $C_{26}H_{29}N_5O_2$

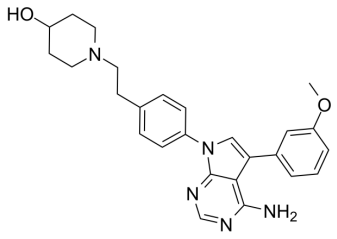
Molecular Weight: 443.54

Target: Src

Pathway: Protein Tyrosine Kinase/RTK

Storage: -20°C, stored under nitrogen

* In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 26.0 mg/mL (58.62 mM; Need ultrasonic and warming)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2546 mL	11.2729 mL	22.5459 mL
	5 mM	0.4509 mL	2.2546 mL	4.5092 mL
	10 mM	0.2255 mL	1.1273 mL	2.2546 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.08 mg/mL (4.69 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

CGP77675 is an orally active and potent inhibitor of Src family kinases. CGP77675 inhibits phosphorylation of peptide substrates and autophosphorylation of purified Src (IC_{50}s of 5-20 and 40 nM, respectively), and also inhibits Src, EGFR, KDR, v-Abl, and Lck with IC_{50}s of 5-20, 40, 20, 150, 1000, 310, and 290 nM, respectively. Anticancer activity[1].

IC_{50} & Target

IC50: 0.02 μM (Src), 0.15 μM (EGFR), 1.0 μM (KDR), 0.31 μM (v-Abl), 0.29 μM (Lck)[1]

In Vitro

CGP77675 dose dependently inhibits phosphorylation of poly-Glu-Tyr with an IC_{50} value of 5.5 nM, and of the optimal Src substrate (OSS) peptide with an IC_{50} value of 16.7 nM. These IC_{50} values are similar to the value obtained with chicken Src (20 nM)[1].

CGP77675 inhibits the parathyroid hormone-induced bone resorption in rat fetal long bone cultures with an IC_{50} of 0.8 μM[1].

CGP77675 (0.04-10 μM; 2 hours) potently inhibits tyrosine phosphorylation of the Src substrates Fak and paxillin, but has much less effect on Src (IC_{50} values 0.2, 0.5, and 5.7μM) in IC8.1 cells[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	MC3T3-E1 cells
Concentration:	0.2, 1, and 5 μM
Incubation Time:	3 days
Result:	Did not influence cell viability for up to 3 days of treatment.

Western Blot Analysis[1]

Cell Line:	Src-overexpressing IC8.1 cells
Concentration:	0.04, 0.2, 1, 5, and 10 μM
Incubation Time:	2 hours
Result:	Dose dependently inhibited phosphorylation of Fak and paxillin, but not of Src.

In Vivo

CGP77675 (1, 5, and 25 mg/kg; injected s.c.; twice a day) inhibits IL-1β-induced hypercalcemia in Mice[1].
CGP77675 (10 and 50 mg/kg; administered orally; twice a day for 6 weeks) partially prevents bone loss and rescues bone microarchitectural features in young ovx rats[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	Male mice (Tif:MAGf; Novartis Animal Farm) of 25-30 g body[1]
Dosage:	1, 5, and 25 mg/kg
Administration:	Injected s.c.; twice a day
Result:	Prevented IL-1β-induced hypercalcemia in mice without affecting serum amyloid protein levels.

Animal Model:	Eight-week-old (175-209 g) female rats of the Sprague-Dawley-derived strain Tif:RAlf[1]
Dosage:	10 and 50 mg/kg
Administration:	Administered orally; twice a day for 6 weeks
Result:	Partly prevented bone loss.

REFERENCES

[1]. Missbach M, et al. A novel inhibitor of the tyrosine kinase Src suppresses phosphorylation of its major cellularsubstrates and reduces bone resorption in vitro and in rodent models in vivo. Bone. 1999 May;24(5):437-49.

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